3-5-96

MEMORANDUM

SUBJECT: PP#5E04566. Abamectin (AGRI-MEK 0.15EC miticide/insecticide, EPA Reg. No. 618-98) in or on Hops. Evaluation of analytical methods and magnitude of residue data.

MRID No. 437331-01, Chemical Code: 122804
CBTS No. 16210, DP Barcode: D219147.

FROM: William D. Wassell, Chemist
Chemistry Branch I - Tolerance Support
Health Effects Division (7509C)

THROUGH: Edward Zager, Acting Chief
Chemistry Branch I - Tolerance Support
Health Effects Division (7509C)

TO: Hoyt Jamerson, PM-43
Emergency Response and Minor Use Section
Registration Division (7505C)

George M. Markle, Associate Director, Interregional Research Project No. 4 (IR-4), State Agricultural Experiment Station, Rutgers University, New Brunswick, NJ on behalf of the IR-4 Project, the Agricultural Experiment Stations of Idaho, Oregon and Washington, the Idaho, Oregon and Washington Hop Commissions and the Hops Growers of America requests the establishment of a tolerance for residues resulting from the use of the miticide/insecticide abamectin [a mixture of avermectins containing ≥80% avermectin B_{1a} (5-O-demethyl avermectin A_{1a}) and ≤20% avermectin B_{1b} (5-O-demethyl-25-de (1-methylpropyl)-25-(1-methylethyl) avermectin A_{1a})] on hops. The tolerance is requested in terms of the combined residues of the insecticide avermectin B_1 and its delta-8,9-isomer in or on the raw agricultural commodity dried hops at 0.2 ppm.

A time-limited tolerance for residues of abamectin and its delta-8,9-isomer on dried hops has been established at 0.5 ppm (61 FR 4593, February 7, 1996). Tolerances have been established for avermectin B_1 and its delta-8,9-isomer on various RACs, processed commodities, and animal feeds (40 CFR §180.449, §185.300, and §186.300, respectively).

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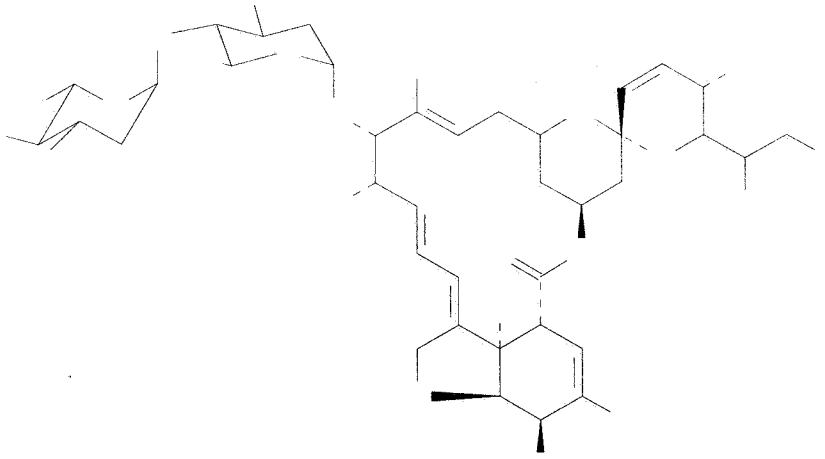
Abamectin is not a FIFRA '88 reregistration pesticide active ingredient.

Associated with this petition are one volume of residue chemistry data which are evaluated in this document. This information was reviewed by Dynamac Corporation under the supervision of CBTS. The data assessment has undergone secondary review in the branch and has been revised to reflect branch policy.

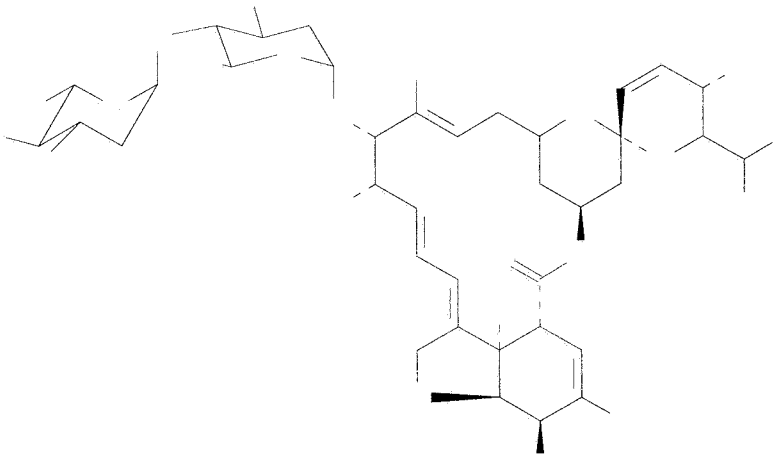
The molecular structures of avermectin B_{1a} and B_{1b} are illustrated in Figure 1.

Figure 1

Avermectin B1a



Avermectin B1b



Executive Summary of Deficencies Remaining to be Resolved:

* Submission of Revised Analytical Method.

Conclusions

1. Data in this petition were generated by Merck Research Laboratories.

2a. Product chemistry data were not submitted with the subject petition. The manufacturing process of technical grade avermectin has been adequately described (see our memo of 5/1/86, L. Cheng, CBRS # 388).

2b. AGRI-MEK 0.15 EC, (EPA Reg. No. 618-98), has been proposed for use on hops. This product contains 0.15 lbs ai/ gallon as a mixture of avermectins containing ≥80% avermectin B_{1a} and ≤20% avermectin B_{1b}. The determination as to whether the inerts contained in the formulated product are cleared under 40 CFR §180.1001 is under the purview of Registration Division.

3. CBTS concludes that the available plant metabolism data are sufficient to support the proposed use on dried hops. The residues of concern are the parent compound (avermectin B_{1a} and B_{1b}) and its delta-8,9-isomer.

4. Animal feed items are not derived from hops. Therefore, there is no concern for the metabolism or magnitude of residues of abamectin in livestock resulting from the proposed use.

5a. Merck Method M-036.1 for analysis of avermectin B_1 and its delta-8,9-isomer in/on dried hops has been adequately validated for collection of residue data on hops.

5b. The petitioner has previously submitted an independent laboratory validation of method M-036 (see our review of 07/26/95, W.D. Wassell, PP#4E4419). Method M-036 has been successfully validated by the Agency's Analytical Chemistry Laboratory. Several minor modifications to the method have been suggested by ACL/BEAD and the petitioner is required to rewrite the method to include these modifications. The petitioner should refer to Deficiencies 4, 6, 7, 8 and 9 of our memo of 02/07/96 (W.D. Wassell, PP#4E4419) for specific instructions concerning rewriting Merck Method M-036.

5c. Residues of abamectin are not recovered by the FDA Multiresidue protocols contained in PAM I.

5d. CBTS concludes adequate methodology for the enforcement of the proposed tolerances for residues of abamectin and its delta-8,9-isomer are not available until the rewritten method (M-036) is submitted.

6. Data reflecting the stability of avermectin B_{1a}, B_{1b} and/or the delta-8,9 isomer of

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avermectin B_{1a} in or on various crops during frozen storage have been submitted previously. CBTS concludes the previously submitted storage stability data are adequate to support the maximum storage interval for samples of the hop residue studies.

7. Magnitude of residue data were submitted with the subject petition. The data indicate that combined residues of avermectin B_{1a} its delta-8,9-isomer and avermectin B_{1b} are not likely to not exceed the proposed tolerance level of 0.20 ppm in/on dried hops following the proposed use. The maximum combined residues in dried hops resulting from the proposed use were $\leq$0.094 ppm.

8. The International Tolerance Status Sheet is attached and there are no established tolerances for abamectin in or on dried hops in Canada, Mexico or Codex. Therefore, there are no compatibility problems.

Recommendations

CBTS cannot recommend in favor of establishment of the proposed tolerance for reasons outlined in 5b and 5d, above. In order to convert the existing time-limited tolerance to a permanent tolerance, deficiencies outlined in our 2/7/96 memo (W.D. Wassell, PP#4E4419) concerning the enforcement method must be addressed.

Detailed Considerations

Manufacturing and Formulation:

Product chemistry data were not submitted with the subject petition. The manufacturing process of technical grade avermectin has been adequately described (see our memo of 5/1/86, L. Cheng, CBRS # 388). AGRI-MEK 0.15 EC, (EPA Reg. No. 618-98), has been proposed for use on hops. This product contains 0.15 lbs ai/ gallon as a mixture of avermectins containing $\geq$80% avermectin B_{1a} (5-O-demethyl avermectin A_{1a}) and $\leq$20% avermectin B_{1b} (5-O-demethyl-25-de (1-methylpropyl)-25-(1-methylethyl) avermectin A_{1a}). The determination as to whether the inerts contained in the formulated product are cleared under 40 CFR §180.1001 is under the purview of Registration Division.

Proposed Use:

For control of Twospotted Spider Mites on hops, apply AGRI-MEK® 0.15 EC (EPA Reg. No. 618-98) as a foliar spray using ground equipment, at the rate of 16 fl. oz./A (0.019 lb ai/A). Do not exceed 32 fl. oz./A/season (0.038 lb ai/A/season). Applications are made in at least 40 gal/A not less than 21 days apart. A 28-day preharvest interval (PHI) is proposed. Do not permit livestock to graze in treated hop yards.
CBTS concludes the directions for use of the product on hops are adequate.

Nature of the Residue - Plants:

No new plant metabolism data were submitted with this tolerance request. Metabolism data have been previously submitted on cottonseed, citrus, and celery (PP#'s 5G3500, 5G3287, and 8F3649, respectively).

In conjunction with PP#1F3973 (see our memo of 11/26/91, G.J. Herndon), CBTS concluded that the available metabolism studies for abamectin on cotton, citrus, and celery were sufficient to support the use of the product on almonds, walnuts, and lettuce. However, it was noted that the petitioner should be prepared to conduct additional plant metabolism studies on other crops to support future uses, especially if the use patterns differ significantly from those of cotton, celery, and citrus. The application rates in the metabolism studies on the above commodities were at 0.6 lbs ai/A to 2.25 lbs ai/A. As the proposed maximum application rate for abamectin on hops is 0.04 lb. ai/A/season, CBTS concludes that the metabolism data are sufficient to support the proposed use on hops. The residues of concern are the parent compound (avermectin B_{1a} and B_{1b}) and its delta-8,9-isomer.

Nature and Magnitude of the Residue - Animals:

Animal metabolism data were not submitted in conjunction with the subject petition. Animal feed items are not derived from hops. Therefore, there is no concern for the metabolism or magnitude of residues of abamectin in livestock resulting from the proposed use.

Analytical Methods - Enforcement and Data Collection:

The analytical portion of the submitted residue trials were conducted by Merck Research Laboratories, Three Bridges, NJ.
The analytical method utilized for the determination of the residue levels in the submitted residue studies is entitled:

> "M-036.1: Liquid Chromatographic Method for the Quantitation of Total avermectin B_1 and 8,9-Z-avermectin B_1 in Dried Hops Using Fluorescence Detection".

Using this method, dried hops are rehydrated and residues are extracted with methanol:water (60:40, v/v). The avermectins are partitioned into hexane and the hexane extract is concentrated and purified on an aminopropyl solid phase extraction column. The residues are derivatized with trifluoroacetic anhydride and analyzed by reversed phase HPLC using fluorescence detection. The limit of quantitation (LOQ) for individual residues of avermectin B_1 and its delta-8,9-isomer is 0.005 ppm. The limit of detection was reported as 0.002 ppm. Method recovery data are summarized in Table 1.

Table 1

Lab Validation of Method M-036 for Avermectin Residues on Dried Hops

compound	spike level (ppb)	% recovery
B_{1a}	5	108
		106
	100	104
		106
	1000	106
		102
B_{1b}	4.9	90
		90
	49	94
		94
Δ-8,9-isomer	5.0	92
		96
	100	88
		80
	1000	73
		80

CBTS concludes Method M-036.1 has been adequately validated for collection of residue data on hops.

The petitioner has previously submitted an independent laboratory validation of method M-036 (MRID 436801-01, see our review of 07/26/95, W.D Wassell, PP#4E4419). Method M-036 has been successfully validated by the Agency's Analytical Chemistry Laboratory. Several minor modifications to the method have been suggested by ACL/BEAD and the petitioner will be required to rewrite the method to include these modifications. The petitioner should refer to Deficiencies 4, 6, 7, 8 and 9 of our memo of 02/07/96 (W.D. Wassell, PP#4E4419) for specific instructions concerning rewriting Merck Method M-036. When the rewritten method is submitted, CBTS will forward it to ACL/BEAD for review/approval prior to submission to the FDA for publication in PAM II.

Residues of abamectin are not recovered by the FDA Multiresidue protocols contained in PAM I.

CBTS concludes adequate methodology for the enforcement of the proposed tolerances for residues of abamectin and its delta-8,9-isomer are not available.

Storage Stability Data:

No storage stability data were provided with this petition. Data reflecting the stability of avermectin B_{1a}, B_{1b} and/or the delta-8,9 isomer of avermectin B_{1a} in or on various crops during frozen storage have been submitted previously. The available data include the following crops and storage periods: pears for one year (see our memo of 7/9/91, J.Stokes, PP#9F3787); celery for two years (see our memo of 5/4/90, S. Willett, PP#8F3649); oranges, lemons and grapefruits for one year (see our memo of 6/21/89, V.F. Boyd, PP#8F3592); tomatoes for six months (see our memo of 12/15/89, S. Willett, PP#9F3703); and cottonseed (parent compound only) for 14 months (see our memo of 7/29/87, C. Deyrup, PP#7F3500).

Samples from the submitted field trials were stored frozen up to 173 days between harvest and analysis. CBTS concludes the previously submitted storage stability data are adequate to support the maximum storage interval for samples of the hop residue studies.

Magnitude of the Residue: (MRID No. 437331-01)

The following field trial data from four sites were submitted with the current petition:

> "Determination of the Magnitude of the Residues of Avermectin B_1 and 8,9-Z Avermectin B_1 in/on the Raw Agricultural Commodity, Dried Hops and in Spent Hops, from Abamectin 0.15 EC Applied by Ground Equipment", R.D. Brown, 6/15/95, (MRID# 437331-01, vols. 1 and 2)."

Data were submitted from four field trials on hops, two in WA and one each in ID and OR. Avermectin was applied twice, 20 days apart, at 0.019 lb ai/application for a total of 0.038 lb ai/A (~1x the proposed rate). Actual application rates ranged from 0.018-0.020 lb ai/A. Applications were made using ground equipment (airblast sprayers) with spray volumes ranged from 47.2-54.8 gal/A. Two replicate samples were collected at each site at each of two PHIs, 0 and 27-28 days. Within 8 hours of sampling, hop cones were dried in a commercial hop drier at 38-46 C in the OR test and 54-65 C in the other tests, to a target moisture of 7-10%. Samples were stored frozen for up to 173 days prior to analysis by Merck Research Laboratories, Three Bridges, NJ. Merck Method M-036.1 was used to quantitate residues of avermectin B_{1a}, its delta-8,9-isomer and avermectin B_{1b}. The residue data are summarized in Table 3. The maximum combined residues of abamectin and its delta-8,9-isomer at the proposed 28-day PHI were 0.094 ppm.

Geographic representation, the number of trials, and number of samples at the proposed use rate are adequate. The data indicate that combined residues of avermectin B_{1a}, its delta-8,9-isomer and avermectin B_{1b} are not likely to not exceed 0.20 ppm in/on dried hops following the proposed use. The maximum combined residues in dried hops resulting from the proposed use were $\leq$0.094 ppm.

Table 3

Abamectin residues in/on dried hops following two foliar applications of the 0.15 lb/gal EC.

State/ Study No.	Spray volume/ application (gal/A)	Rate/ application (lb ai/A)	Total Rate (lb ai/A)	PHI (days)	Residues (ppm)[a]		
					B_1a	B_1b	Total
WA 001-94-100 5R	50.1	0.019	0.038	0	0.591 0.728	0.059 0.073	0.650 0.801
				27	0.044 0.078 0.086 0.082	<0.005 0.008 0.0075 0.0073	<0.049 0.086 0.094[b] 0.089[b]
WA 001-94-100 6R	50.3	0.019	0.038	0	0.161 0.151	0.015 0.015	0.176 0.166
				28	0.017 0.023	<0.002 <0.002	<0.019 <0.025
ID 001-94-100 7R	49.4	0.019	0.038	0	0.673 0.592	0.072 0.064	0.745 0.656
				28	0.055 0.057	<0.005 <0.005	<0.060 <0.062
OR 001-94-100 8R	52.0	0.019	0.038	0	0.968 0.810	0.096 0.081	1.064 0.891
				28	0.009 0.015	<0.002 <0.002	<0.011 <0.017

[a] Residues are not corrected for method or storage recoveries.
[b] These samples were used in the hops processing study.

Processed Food/Feed:

Dried hops from one of the tests conducted in WA (Study No. 001-94-1005R) were subjected to laboratory processing in order to produce spent hops for residue analysis. CBTS no longer requires residue data for spent hops. Therefore, this data will not be discussed in this review.

Other Considerations - Harmonization of Tolerances:

The International Tolerance Status Sheet is attached and there are no established tolerances for abamectin in or on dried hops in Canada, Mexico or Codex. Therefore, there are no compatibility problems.

Attachment (1): 1. IRL Status Sheet

cc: WDWassell, RF, Circ., Avermectin SF, PP#4E4419.

RDI: RALoranger: 03/05/96; EZager: 03/05/96.
7509C:CBTS:WDWassell:wdw:CM#2:Rm 804U:305-6135:03/05/96
Disk: WDW-6, File: FY96WDW.148

Residue Chemistry Review

Subject: **PP#5E04566. Abamectin (AGRI-MEK 0.15EC miticide/insecticide, EPA Reg. No. 618-98) in or on Hops. Evaluation of analytical methods and magnitude of residue data. MRID No. 437331-01, Chemical Code: 122804 CBTS No. 16210, DP Barcode: D219147.**

Document Class:

Product Chem:

Residue Chem:
860.1200 Directions for use
860.1340 Residue analytical method
860.1500 Crop field trials
860.1550 Proposed tolerances

Biochemicals:

DP Barcode: D219147

MRIDs: 43733101

PC Codes: Actives 122804 Abamectin (ANSI)
Inerts

Commodities: Hops

Administrative #: 5E04566; 000618-00098

Reviewers: William D. Wassell

Review Approver: Edward Zager **Approved on:** March 5, 1996

WP Document: Abamecti.054

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